

## CLAIMS

What Is Claimed Is:

1. A combinatorial library of indolinone compounds, comprising a series of at least ten indolinones that can be formed by reacting oxindoles with aldehydes.

2. The combinatorial library of claim 1 wherein said oxindoles are type A oxindoles.

3. The combinatorial library of claim 1 wherein said aldehydes are type B aldehydes.

4. The combinatorial library of claim 1 wherein said library comprises at least 100 indolinones.

5. The combinatorial library of claim 1 wherein said library comprises at least 1000 indolinones.

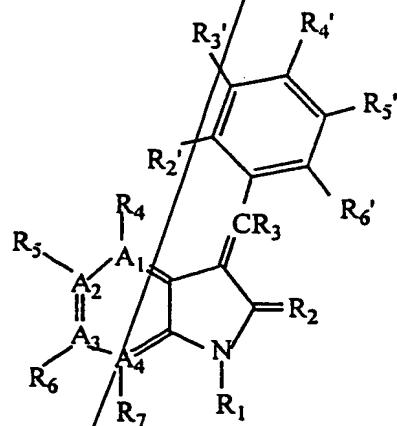
6. The combinatorial library of claim 1, wherein most of said indolinones are in the cis conformation.

7. A method of making an indolinone comprising the steps of  
(a) creating a combinatorial library of

indolinones by reacting a series of oxindoles with a series of aldehydes,

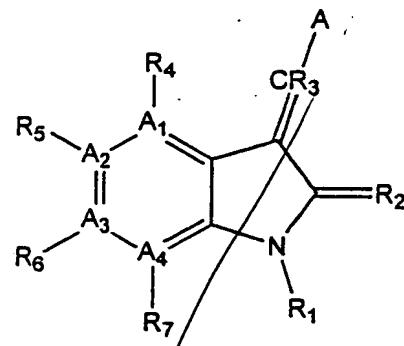
- (b) testing said indolinones in biological assays,
- (c) selecting one or more indolinones with favorable activity; and
- (d) synthesizing one or more of said indolinones selected in step (c).

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8. A compound having formula V or VI



(V)

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(VI)

*Seth BP*

and pharmaceutically acceptable salts, isomers,  
metabolites, esters, amides, and prodrugs thereof, wherein:

- (a)  $A_1$ ,  $A_2$ ,  $A_3$ , and  $A_4$  are independently carbon or nitrogen;
- (b)  $R_1$  is hydrogen or alkyl;
- (c)  $R_2$  is oxygen or sulfur;
- (d)  $R_3$  is hydrogen;
- (e)  $R_4$ ,  $R_5$ ,  $R_6$ , and  $R_7$  are optionally present and are each independently selected from (i) the group consisting of hydrogen, alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl,  $S(O)R$ ,  $SO_2NRR'$ ,  $SO_3R$ ,  $SR$ ,  $NO_2$ ,  $NRR'$ ,  $OH$ ,  $CN$ ,  $C(O)R$ ,  $OC(O)R$ ,  $NHC(O)R$ ,  $(CH_2)_nCO_2R$ , and  $CONRR'$  or (ii) any two adjacent  $R_4$ ,  $R_5$ ,  $R_6$ , and  $R_7$ , taken together form a fused ring with the aryl portion of the oxindole-based portion of the indolinone;
- (f)  $R_2'$ ,  $R_3'$ ,  $R_4'$ ,  $R_5'$ , and  $R_6'$  are each independently

selected from the group consisting of hydrogen, alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl, S(O)R, SO<sub>2</sub>NRR', SO<sub>3</sub>R, SR, NO<sub>2</sub>, NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, (CH<sub>2</sub>)<sub>n</sub>CO<sub>2</sub>R, and CONRR';

5 (g) n is 0, 1, 2, or 3;  
(h) R is H, alkyl or aryl; and  
(i) R' is H, alkyl or aryl.  
10 (j) A is a five membered heteroaryl ring selected from the group consisting of thiophene, pyrrole, pyrazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, oxazole, isoxazole, thiazole, isothiazole, furan, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3,4-oxatriazole, 1,2,3,5-oxatriazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole, 1,2,3,4-thiatriazole, 1,2,3,5-thiatriazole, and tetrazole, optionally substituted at one or more positions with alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl, S(O)R, SO<sub>2</sub>NRR', SO<sub>3</sub>R, SR, NO<sub>2</sub>, NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, (CH<sub>2</sub>)<sub>n</sub>CO<sub>2</sub>R or CONRR'.  
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9. A pharmaceutical composition comprising a pharmaceutically acceptable carrier or excipient and a compound according to Claim 8.

10. A method for treating diseases related to unregulated tyrosine kinase signal transduction, the method  
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comprising the step of administering to a subject in need thereof a therapeutically effective amount of a compound according to Claim 8.

11. A method for regulating tyrosine kinase  
5 signal transduction comprising administering to a subject a therapeutically effective amount of a compound according to Claim 8.

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